**Supplementary Information**

**An *in silico* predictive method to select multi-monomer combinations for peptide imprinting**

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**Table 1S: Grid dimensions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Peptide** | **Autodock 4.2.6 and Autodock Vina** | | **Glide** | |
| **Grid size** | **Grid center** | **Grid size** | **Grid center** |
| **Peptide 1** | **46, 54, 68** | **29.878, 28.375, 30.905** | **30, 30, 30** | **32, 32, 34** |
| **Peptide 2** | **58, 40, 56** | **29.671, 29.81,29.812** | **30, 30, 30** | **38, 35.56, 37.77** |
| **Peptide 3** | **66, 72, 40** | **36.936, 36.864, 36.821** | **30, 30, 30** | **36, 35, 30** |

Table 1S: Grid dimensions used for peptides 1,2 and 3 in the softwares Autodock 4.2 ,Vina and Glide. These are given in the order of x, y and z coordinates.

**Table 2S: Functional monomer combinations**

|  |  |  |  |
| --- | --- | --- | --- |
| **Entry** | **TBAm** | **Aac** | **APMA** |
| 1. | 40 | 0 | 5 |
| 2. | 40 | 10 | 5 |
| 3 | 40 | 15 | 5 |
| 4 | 40 | 5 | 0 |
| 5 | 40 | 5 | 10 |
| 6 | 40 | 5 | 15 |
| 7 | 0 | 5 | 5 |
| 8 | 55 | 5 | 5 |
| 9 | 65 | 5 | 5 |

*Table 2S: Ratio of functional monomers (mol%) employed for optimization of polymer composition in the reference article by Bedwell et al.*1 *Final mol% made upto 100% with NIPAM*.

**Figure 1S: Predicted local structure profile**

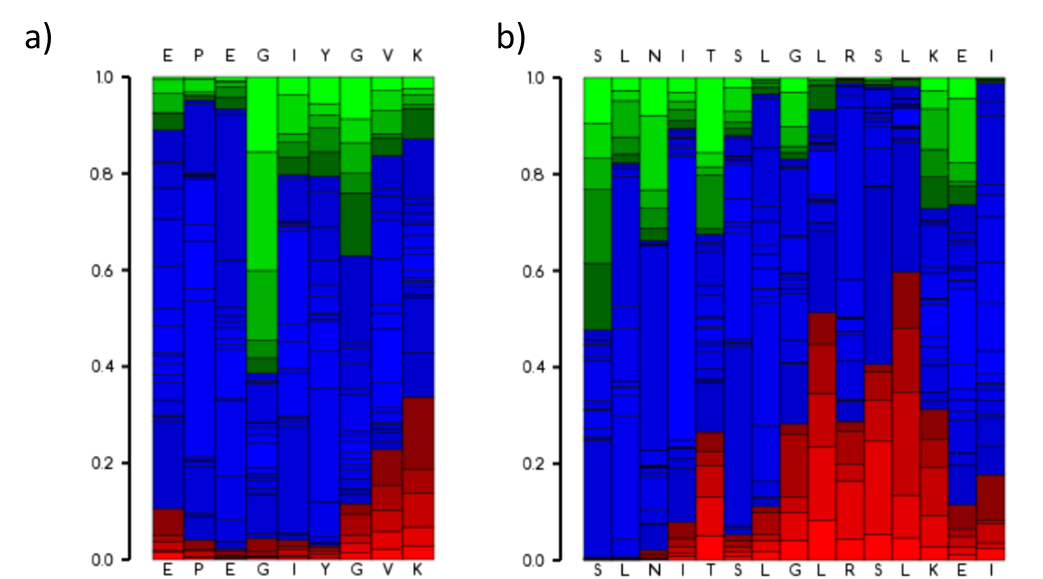


Figure 1S: Predicted local structure profile using PEP-Fold3 2. The probabilities, at each position of the sequence, are sorted from helical (red), coil (blue) to extended (green). This is based on structural alphabets that are 4 residues long, so the profile is of the size of the amino acid sequence minus 3.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Peptide** | **Multi-Monomer Simultaneous Docking** | | | | **Single Monomer Docking**  **With NIPAM** |
| **APMA+NIPAM** | **AA + NIPAM** | **TBAM+NIPAM** | **AA +APMA +TBAm+NIPAM** |
| **Peptide 1** | -4.64 (APMA),  -3.69 (NIPAM) | -2.84(AA),  -3.69(NIPAM) | -4.01(TBAm),  -3.69 (NIPAM) | **-2.84**(AA),  -4.55 (APMA),  -4.02 (TBAm),  -3.67(NIPAM) | -2.84 (AA),  -4.66 (APMA),  -4.02 (TBAm),  -3.69(NIPAM) |
| **Peptide 2** | -4.76 (APMA),  -3.69 (NIPAM) | -2.70 (AA),  -3.69 (NIPAM) | -4.02 (TBAm),  -3.69 (NIPAM) | -2.69(AA),  -4.65 (APMA),  -4.02 (TBAm),  -3.69(NIPAM) | -2.73 (AA),  -4.77 (APMA),  -4.02 (TBAm),  -3.69 (NIPAM) |
| **Peptide 3** | -3.25(APMA),  - 2.58(NIPAM) | -2.90 (AA),  -2.56 (NIPAM) | -2.56(TBAm),  -2.57 (NIPAM) | -2.90(AA),  -3.36 (APMA),  -2.56 (TBAm)  -2.59(NIPAM) | -2.91 (AA),  -3.39 (APMA),  -2.56 (TBAm),  -2.59 (NIPAM) |

Table 2S: Estimated binding energy (kcal/mol) for each monomer in multi-monomer combinations and single monomer docking considering NIPAM as the fourth monomer in the pre-polymerization mixture. Decrease in binding energies relative to each other are highlighted in red to represent the effect of NIPAM in MMSD combination compared to SMD. Higher negative binding energy values represent higher binding affinity with the respective peptide. No polymer composition without NIPAM is employed therefore the comparison cannot be appropriately concluded.

|  |  |
| --- | --- |
| Peptide | Binding Energy (kcal/mol) |
| Peptide 1 | -3.92 |
| Peptide 2 | -3.93 |
| Peptide 3 | -2.63 |

Table 3S: Docking scores with Bisacrylamide crosslinker as part of the pre-polymerization mixture. The mol% is kept constant (2%) in all the polymer combinations and also, since no control polymer is possible without the cross linker, therefore only single monomer docking is used to reflect on the cross-linker-peptide interactions.

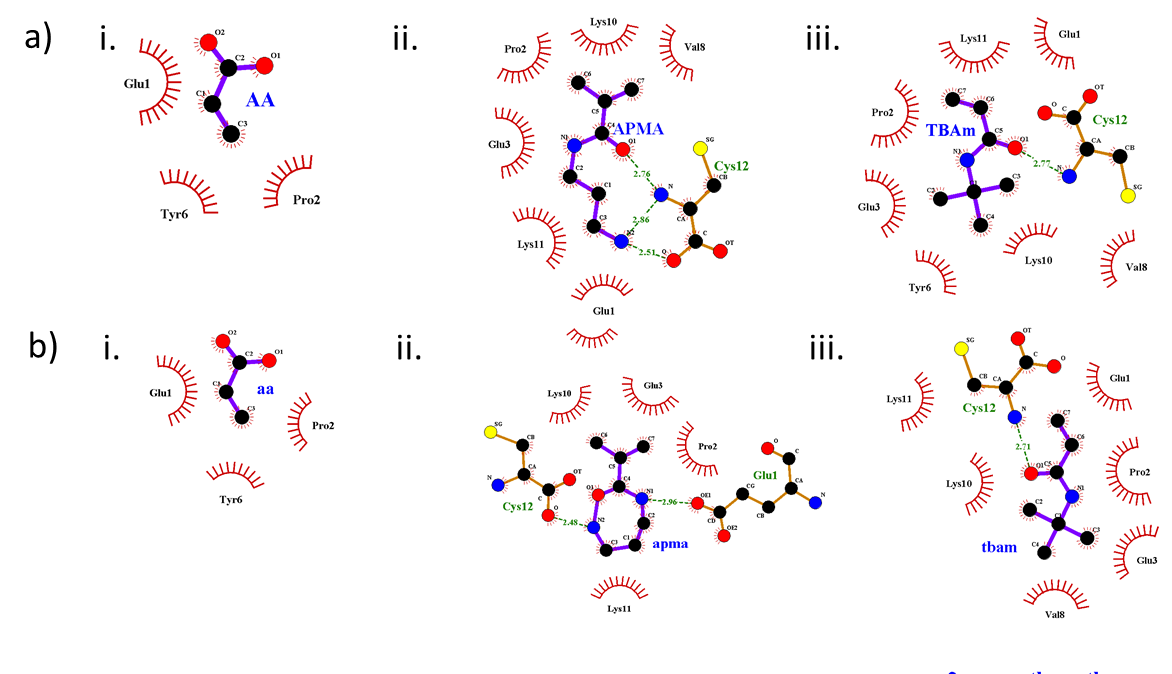
**Figure 2S: 2D interaction maps for peptide 2**

Figure 2S: 2D interaction maps representing monomer interaction with peptide 2, generated using LigPlot. Interactions resulting from single monomer docking of AAc, APMA and TBAm are shown in a-i, ii and iii, respectively. Multi-monomer simultaneous docking outcomes are shown for tri-monomer combination (AAc+APMA+TBAm) (b). Monomers are marked in capital when docked individually and in small letters, when used in MMSD. Green lines indicate H-bonding and red lines indicate hydrophobic interactions with the respective amino acids. The heteroatoms like N, O and S are represented by blue, red and yellow spheres, respectively.

**Figure 3S: 2D interaction maps for peptide 3**

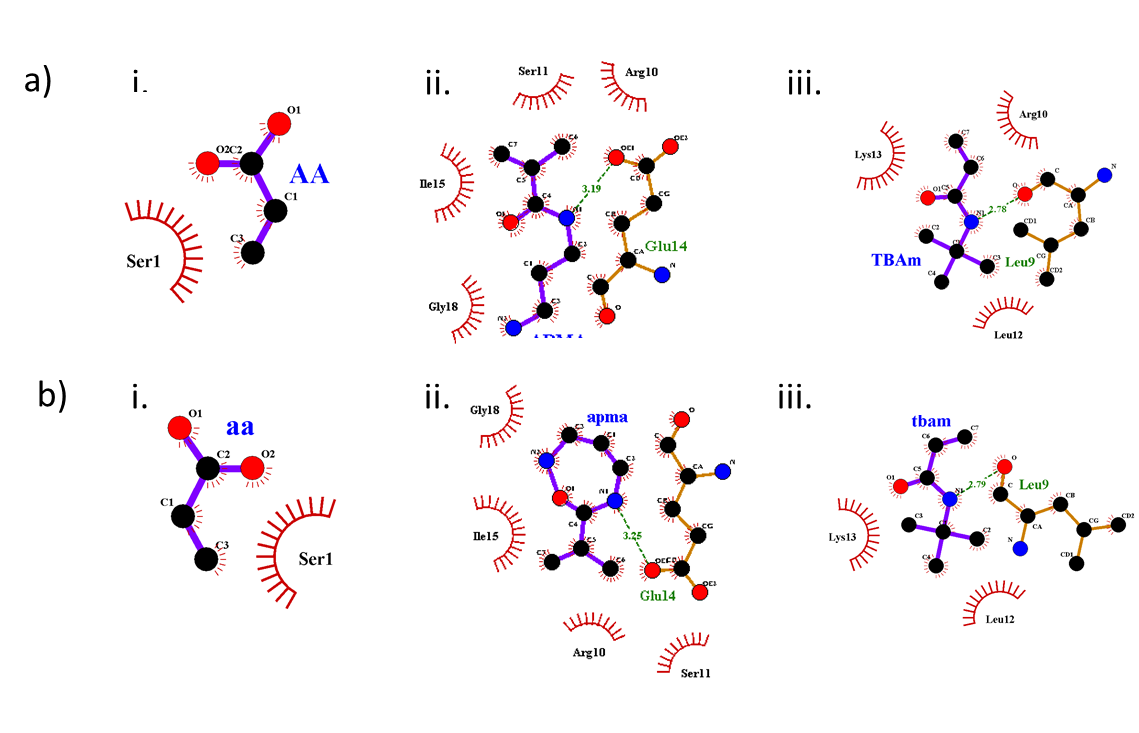


Figure 3S: 2D interaction maps representing monomer interaction with peptide 3, generated using LigPlot. Interactions resulting from single monomer docking of AAc, APMA and TBAm are shown in a-i, ii and iii, respectively. Multi-monomer simultaneous docking outcomes are shown for tri-monomer combination (AAc+APMA+TBAm) (b). Monomers are marked in capital when docked individually and in small letters, when used in MMSD. Green lines indicate H-bonding and red lines indicate hydrophobic interactions with the respective amino acids. The heteroatoms like N, O and S are represented by blue, red and yellow spheres, respectively.

**References**

1 T. S. Bedwell, N. Anjum, Y. Ma, J. Czulak, A. Poma, E. Piletska, M. J. Whitcombe and S. A. Piletsky, *RSC Adv.*, 2019, **9**, 27849–27855.

2 A. Lamiable, P. Thévenet, J. Rey, M. Vavrusa, P. Derreumaux and P. Tufféry, *Nucleic Acids Res.*, 2016, **44**, W449–W454.